IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No.	: 10/562,698	Confirmation No.	: 4276
First Named Inventor	: Jeewoo LEE		
Filed	: July 2, 2004		
TC/A.U.	: 1621		
Examiner	: Peter G. O'Sullivan		
Docket No.	: 106930.57239US		
Customer No.	: 23911		
Title	: 4-(Methyl Sulfonyl Amino) Phenyl Analogues as Vanilloid Antagonist Showing Excellent Analgesic Activity and the Pharmaceutical Compositions Comprising the Same		

DECLARATION UNDER 37 C.F.R. § 1.132

Commissioner for Patents
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I, Jeewoo Lee, hereby declare as follows:

1. I am a citizen of Korea, residing at 27-901 Misung Apt, Apgujung-Dong, Kangnam-Gu, Seoul, Korea.

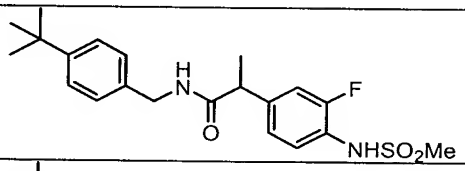
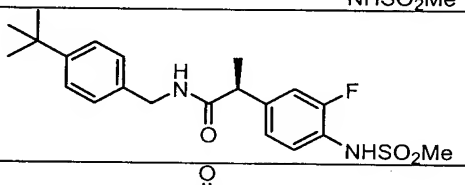
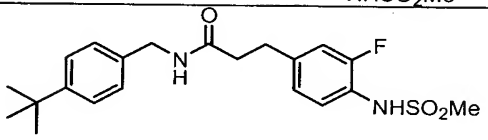
2. I graduated from Seoul National University in 1983. I also have a Master's Degree from Seoul National University. I subsequently studied medicinal chemistry at the Department of Medicinal Chemistry at the State University of New York in Buffalo, New York and was awarded a Ph.D. degree in medicinal chemistry from the State University of New York in Buffalo, New York in 1991.

3. I have 28 years experience in the field of medicinal chemistry including five years as a chemistry researcher at the National Cancer Institute in Bethesda, Maryland where I designed and synthesized novel analgesic and anticancer drugs. For the past 16 years I have been employed by Seoul National University as a Professor. In addition, in 2000 I founded a pharmaceutical research and development company, Digital Biotech, where I actively participate in new drug development. I have particular experience in optimizing lead compounds for activity, toxicity and pK.

4. I am an inventor of the invention described and claimed in the above-identified U.S. patent application no. 10/562,698 and make this declaration in support of said patent application which claims compounds exhibiting outstanding antagonistic activity against the vanilloid receptor (TRPV1).

5. I have reviewed in detail the Office Action dated November 16, 2009, from which I understand that claims 15-17 and 22-29 of said patent application have been rejected as obvious in view of published PCT patent application no. WO 2002/016318 ("Suh et al."). The rejection is based in particular on the compound of Suh et al.'s Example 168, which I believe to be the closest prior art to the novel compounds claimed in application no. 10/562,698.

6. Under my direction and supervision, the compound according to the present invention N-(4-tert-butylbenzyl)-2-[3-fluoro-4-(methylsulfonylamino)-phenyl]propionamide and its stereospecific S-isomer, N-(4-tert-butylbenzyl)-2(S)-[3-fluoro-4-(methylsulfonylamino)phenyl]propionamide, as well as the compound of Suh's Example 168, were tested for antagonistic activity against the human vanilloid receptor (hTRPV1). The structural formulas of the tested compounds and the test results are shown in the following table:

Compound	Structure	K_i (antagonism) (hTRPV1)
N-(4-tert-butylbenzyl)-2-[3-fluoro-4-(methylsulfonylamino)phenyl]propionamide		35 nM
N-(4-tert-butylbenzyl)-2(S)-[3-fluoro-4-(methylsulfonylamino)phenyl]propionamide		20 nM
Compound of Example 168		>10,000 nM

6. The experimental test results show that the compound according to the present invention, and particularly its S-isomer, exhibit outstandingly superior

human vanilloid receptor antagonistic activity with K_i's of 35 nM and 20 nm, respectively. In contrast, the structurally similar (isomeric) compound of Suh et al.'s Example 168 exhibits no significant human vanilloid receptor antagonistic activity with a K_i of >10,000 nM.

7. A skilled medicinal chemist would expect structurally similar compounds to exhibit similar pharmacological activities. Consequently, in light of the negligible human vanilloid receptor antagonistic activity of Suh et al.'s compound 168, the outstandingly superior human vanilloid receptor antagonistic activity of the compounds of the present invention must be regarded as an unexpected and surprising superior result. There is no way a person skilled in the pharmaceutical arts could have expected or predicted the suprisingly high vanilloid receptor antagonistic activity of the compounds of the invention based on the disclosure of Suh et al. and the general knowledge of the art.

10. All statements made herein of my own knowledge are true, and all statements made on information and belief are believed to be true; and further these statements were made with the knowledge that willful false statements and the like, so made, are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code.

Date: AUG 1, 2011

Jeewoo Lee